# EVTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/41883

A. CLASSIFICATION OF SUBJECT MATTER
IPC($ : CI2Q 1/68; C07H 21/04
US CL : 435/6; 435/91.2
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6; 435/91.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN: medline caplus pubmed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | CHOE et al. The Calcium Activation of Gelsolin: insights from the 3A Strucuture of the G4-G6/Actin Complex; J. MoI. Biol. 2002 324, 691-702. | 1-15 |
| X,P | Database Genbank on NCBI, US National Library of Medicine.(Bethesda, MD, USA) No. NMJ)OO 177 Homo sapiens gelsolin, transcript variant 1, mRNA. 06 Nov. 2005 | 1-1 5 |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
20 January 2006 (20.01.2006)

Date of mailing of the international search report
09 MAR 2006

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Form PCT/ISA/210 (second sheet) (April 2005)

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/41883

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: claims 1-15 SEQ ID NO:1

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group 1, claims 1-15, drawn to a method of determining the level of expression of one or more genes between different samples wherein the one or more genes are selected from nucleotides SEQ ID NOS: 1-19 and polypeptides 20-37.

Group 2, claims 16-19, drawn to kits and an array comprising probes from the genes enumerated in SEQ ID NO: 1-19 and the polypeptides of SEQ ID NO: 20-37.

Group 3, claims 20-22, drawn to a test kit comprising an antibody that specifically binds a polypeptide selected from SEQ ID NOS: 20-37.

Further species election:

For groups 1-3 the species of the groups are considered each of the 19 separately recited sequences for the polynucleotides and 18 separately recited amino acids that correspond to the gene or gene products being measured in the method of group 1 recited in SEQ ID NOS: 1-19 and corresponding 20-37.

The first named invention which will be searched is Group 1, claims 1-15, with respect to the first named species which is the polynucleotide of SEQ ID NO:1 as it relates to the method of Group I.

The inventions listed as Groups 1-3 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The technical feature that joins all of these inventions is that they encompass steps that involve/are involved in the detection of gene expression involved in the detection of cancer. However, a method of detecting differentially expressed genes in cancer was known at the time the invention was made and thus, this is not a special technical feature in view of the PCT rules. In addition, SEQ ID NO:1 that represents the special technical feature of Group II, also known as, Genbank ID NM_000177, was also known in the prior art(see for example JMB (2002)324, 691-702). Group I is the first named invention including a method of determining the level of expression of one or more genes between different samples. Group II is drawn to kits and an array comprising probes from the genes enumerated in SEQ ID NO: 1-19. However, not only are each of these special technical features of groups I and II not the same and shared between the two groups, they were also both already known in the prior art. There is no special techncial feature that joins the first named method and first named product as the product and method of group 1 is anticipated in the prior art. For example, US Patent Publication 2002/0004239 Al by Kaufman et al. teach a method of detecting genes differentially expressed in breast cancer and therefore teach the special technical feature of group I. The remaining groups include additional products and methods that are not linked by a unifying inventive concept as they are drawn to unique products and methods and are so separately grouped.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each is drawn to a unique nucleic acid sequence that does not share a common structure with the others. In addition, each nucleic acid, polypeptide and antibody all consist of different physical structures. For example while the polynucleotides are composed of a chain of nucleic acids linked by phosphodiester bonds. The polypeptides are composed of amino acids linked in peptide bonds

and arranged spatially in a number of different tertiary structures including alpha helices, beta-pleated sheets, and hydrophobic loops (transmembrane domain). Furthermore the antibody of Group III is composed of amino acids linked in peptide bonds and arranged spatially in a very specific tertiary structure that allows that antibody to specifically bind to particular regions, i.e. epitopes, of the encoded polypeptide. Further, antibodies are glycosylated and their tertiary structure is unique, where four subunits (2 light chains and 2 heavy chains) associated via disulfide bonds into a Y-shaped symmetric dimer. As a result each has a different structure and do not relate to a single general inventive concept